

Supplementary Table 1

List of all primary samples used in this study

Sample ID	Line (Coriell Biorepository)	Sex	Age at Sampling	Genotype	Disease	Onset	Upper CAG
HD.44	GM02173	Female	52	HD	Symptomatic	NR	44
HD.45	GM04230	Male	55	HD	Symptomatic	NR	45
HD.46	GM04194	Female	60	HD	Symptomatic	NR	46
HD.47	GM04198	Female	63	HD	Symptomatic	NR	47
HD.42	GM04196	Female	51	HD	Symptomatic	NR	42
HD.40	ND33947	Female	71	HD	Symptomatic	63	40
HD.43	ND30013	Male	54	HD	Symptomatic	50	43
HD.1	GM02147	Male	55	HD	Symptomatic	NR	NR
HD.180	GM09197	Male	6	HD	Symptomatic	<6	180
HD.50	GM04687	Female	37	HD	Symptomatic	27	50
Pre-HD.42	GM04717	Female	44	HD	Pre-symptomatic	60	42
Pre-HD.45	GM04861	Male	16	HD	Pre-symptomatic	33	45
Pre-HD.47	GM04855	Male	11	HD	Pre-symptomatic	26	47
Pre-HD.43	GM04831	Male	23	HD	Pre-symptomatic	40	43
Pre-HD.49	GM04853	Male	15	HD	Pre-symptomatic	30	49
Pre-HD.47b	GM04829	Female	21	HD	Pre-symptomatic	34	47
Ctrl.17	AG04148	Male	56	Control	Healthy	N/A	17
Ctrl.17b	GM02171	Female	22	Control	Healthy	N/A	17
Ctrl.18	F09-238	Female	42	Control	Healthy	N/A	18
Ctrl.19	ND34769	Female	68	Control	Healthy	N/A	19
Ctrl.16	AG11357	Female	62	Control	Healthy	N/A	16
Ctrl.15	AG11483	Female	51	Control	Healthy	N/A	15
Ctrl.1	GM05879	Female	48	Control	Healthy	N/A	NR
Ctrl.2	AG16409	Male	12	Control	Healthy	N/A	NR
Ctrl.3	AG08816	Male	39	Control	Healthy	N/A	NR
Ctrl.4	AG09599	Female	30	Control	Healthy	N/A	NR
Ctrl.20	AG05265	Female	61	Control	Healthy	N/A	20
Ctrl.18b	AG04062	Male	31	Control	Healthy	N/A	18
Ctrl.17c	AG04060	Male	44	Control	Healthy	N/A	17
HD.50 iPSC	ND42235	Derived from HD.50					
HD.40 iPSC	ND33947	Derived from HD.40 in house					

Supplementary Table 2

Analysis of 7 Symptomatic HD and 5 healthy control MSNs
 FDR 0.01 Log Fold-change cutoff 0.5, EdgeR
 GO Analysis performed with MetaCore

	Network Objects	P-value	FDR
Cell differentiation	ACTA2,ACTA1,ADCY1,SERPINA1,ADRA2A,ADRA2C,ANGPT1,ANK1,BCO2,ADRB2,TNFSF9,CD24CRLF1,CNTN1,CPEB1,CPS1,CSF2RB,CSPG4,CYP3A5,CHGA,DAB1,DIO2,DISP1,CTNND2,EDNR A,EDNRB,EGFR,ETV1,ESR1,EDN1,EPHB1,FOXP2,FSHR,FN1,FZD1,CSF3,GNAI1,GNAO1,GABRA 1,GATA3,GDNF,GLI3,GLI3,AVPR2,GRIA2,GUCY1A2,GUCY1A3,HEY2,HHIP,HIST1H4A,IGF1,IL12 A,IL18,INSIG1,ITPR1,ITPR2,LRAT,NR1H3,MYLK,MMP9,MYL12A,OPRM1,ONECUT2,OXSR1,OT X1,OSM,PAX3,PDE3B,PDE4A,PDGFB,PDGFR,PRKACA,PLCB1,PLCB1,PGF,PPP2R2A,PCK1,PTAF R,SPI1,PTH,HMMR,RICTOR,RYR2,SCD,PTPN11,SIRPA,SOX2,SREBF1,TBX3,TEC,TGM1,TYRP1,T IAM1,NTRK2,VAV3,WNT1,NCF2	1.51E-10	9.94E-09
Neurotransmission	CHRM2,AKAP5,AOC3,SNAP91,ACTA2,ADCY2,ADCY8,SNCA,BSN,CACNA1G,DLG2,CPLX1,CPLX2 ,DLGAP1,EGFR,ESR1,EPHB1,GNAO1,GAL3ST1,GABRA1,GABRA2,GABRA4,GABRB2,GABRB3,G ABRG1,GABRG2,ABAT,GLRA1,GLRA2,GLRA3,GRID2,GRIA1,GRIA2,GUCY1A2,GUCY1A3,GUCY1 B3,HPCA,HAP1,IGF1,ITPR2,KCNH7,KCNQ2,KCNJ12,MAP1B,MAP2,KCNMA1,OPRM1,NAT2,NP TX2,NPTXR,OR4F14P,PCSK1,PCSK2,PTGER4,PRKACB,PLCB1,PPP2R2B,RYR2,SMPD3,SULT1E 1,SYP,SYN1,SYT1,TMEM108,TRPC6,NTRK2,RAPGEF4,GRM1,GRM5	1.31E-08	4.32E-07
Calcium signaling	CHRM2,AKAP2,ACTA2,ADCY2,ADCY8,ANGPT1,ANK1,PPP1R14A,EGFR,ESR1,GNAO1,GABRB2, GABRB3,ADRB2,GRIA1,GRIA2,GUCY1A2,GUCY1A3,GUCY1B3,HAND1,HAND2,HOXD10,HPD,IG F1,ITPR2,MAP2,MYLK,MMP9,MYL9,MYH15,MYH3,PDE3B,PGF,PRKACB,PKIA,PLCB1,PPP2R2B ,PTAFR,RYR2,SYP,TGM1,TRPC6,TIAM1,VAV3,RAPGEF4,GRM1	5.31E-06	5.01E-05
Huntington Disease	CHRM2,AKAP5,SNAP91,ACTA2,ADCY2,ADCY8,SNCA,BSN,CACNA1G,CD74,CASP10,DLG2,CPLX 1,CPLX2,DAB1,DLGAP1,CTNND2,EGFR,ELOVL7,ENPP2,ESR1,EDN1,EFNA1,EPHA5,EPHA6,EP HA8,FADS1,FADS2,FN1,GNAO1,GABRA1,GABRA2,GABRA4,GABRB2,GABRB3,GABRG1,GABRG 2,ABAT,ADRB2,GRIA1,GRIA2,GUCY1A2,GUCY1A3,GUCY1B3,HPCA,HPD,HAP1,IGF1,ITPR2,KYN U,MAP1B,MMP9,MYL9,MSRA,NPTX2,NPTXR,PRKACB,PLCB1,PPP2R2B,PTAFR,SPI1,PTN,RELB ,SYP,SIRPA,SEMA3A,SYN1,SYT1,TDO2,TMEM108,TRPC6,TXNIP,TIAM1,NTRK2,VAV3,RAPGEF 4,GRM1,GRM5,NCF2	7.22E-04	3.18E-03
Cell cycle and its regulation	ATF3,ADCY2,ADCY8,ADRB2,SMC2,CENPF,CIT,DISP1,EGFR,ESR1,EDN1,GNAO1,GATA3,GDNF,G LI3,GEM,HHIP,HIST1H1D,ITPR2,MARK1,MCM10,MYLK,MMP9,MYL9,OSR1,PAX3,PDGFB,SERP INF1,PRKACB,PLCB1,PGF,PPP2R2B,PCK1,HMMR,FYB,SCD,SYP,SOX2,SREBF1,TBXA2R,TEC,CH RNB2	3.36E-03	1.01E-02
Apoptosis	AOC3,HAP1,ATF3,ADCY2,ADCY8,ANGPT1,TNFSF13B,ADRB2,CD24,CSF2RB,CDH12,CASP10,CI T,DISP1,TNFRSF10B,EGFR,ENPEP,ESR1,EDN1,FN1,CSF3,GNAO1,GAL3ST1,GATA3,GDNF,GLI3, GUCY1A3,GUCY1B3,HHIP,HIST1H1D,HIST1H2BH,IGF1,IL12A,IL18,ITPR2,MARK1,MYLK,MMP 9,MYL9,OSR1,OSM,PAX3,PDGFB,SERPINF1,PRKACB,PLCB1,PPP2R2B,SYP,PCK1,PTAFR,HMM R,RELB,FYB,SCD,SIRPA,SMPD3,SOX2,SREBF1,THBS1,TIAM1,NTRK2,VAV3,CHRN2,NCF2	1.19E-02	3.07E-02

Supplementary Table 3

Target (FW -Forward, RV-Reverse)	Primer Sequence (5'-3')
EMX2 FW	CGGCACTCAGCTACGCTAAC
EMX2 RV	CAAGTCCGGGTTGGAGTAGAC
NEUROG1 FW	GCTCTGACCCAGTAGC
NEUROG1 RV	GCGTTGTGGAGCAAGTC
NEUROD1 FW	GCCCCAGGGTTATGAGACTA
NEUROD1 RV	TCTGTCCAGCTTGGAGGAC
NEUROD6 FW	ACACTACCGTTTGTGAGTCTGT
NEUROD6 RV	CTTCTGGTCTCGCATTCTCT
DARPP-32 FW	TCTCAAGTCGAAGAGACCCAAC
DARPP-32 RV	TGCAGGTGAGACTCAGCAA
HSPA8 FW	ACCTACTCTTGTGTGGGTGT
HSPA8 RV	GACATAGCTTGGAGTGGTTCG
HSPA5 FW	CATCACGCCGCTCTATGTGC
HSPA5 RV	CGTCAAAGACCGTGTCTCG
DNAJB2 FW	ATGGCATCCTACTACGAGATCC
DNAJB2 RV	GAGAGCCTTGCGCCGATAC
DNAJC5 FW	GGGAGTCATTGTACCACGTCC
DNAJC5 RV	CGTGCGCGTTGTTGATCTC
HSPB1 FW	ACGGTCAAGACCAAGGATGG
HSPB1 RV	AGCGTGATTTCCGCGTGA
HSF1 FW	CCATGAAGCATGAGAATGAGGC
HSF1 RV	CTTGTGACGACTTCTCTGTTGC
ATG5 FW	AAAGATGTGCTTCGAGATGTGT
ATG5 RV	CACTTTGTCAATTACCAACGTCA
ATG7 FW	CAGTTTGCCTTTTAGTAGTGC
ATG7 RV	CCAGCCGATACTCGTTCAGC
ATG12 FW	CTGCTGGCGACACCAAGAAA
ATG12 RV	CGTGTTGCTCTACTGCCC
CRYAB FW	CCTGAGTCCCTTACCTTCG
CRYAB RV	CACATCTCCAAACCTTAACTT
VCP FW	CAAACAGAAGAACCGTCCCAA
VCP RV	TCACCTCGGAACAACCTGCAAT
STUB1 FW	AGCAGGGCAATCGTCTGTTC
STUB1 RV	CAAGGCCCGTTGGTGAATA
RPS27A FW	CTGGAAGATGGACGACTTTTGTG
RPS27A RV	CGACGAAGGCGACTAATTTTGC
UBA1 FW	TCGCCGCTGTCCAAGAAAC
UBA1 RV	AGTAAAGGCCCTCGTCTATGTC
UBE3A FW	CTCAGCTTACCTTGAGAACTCG
UBE3A RV	TTCTAGCGCCTTCTTGTTCAT
PSMA3 FW	GCTCAATCGGCACTGGGTAT
PSMA3 RV	ACCTGCTACTGCCATTCCAAC
PSMB6 FW	GGCTACCTTACTAGCTGCTCG
PSMB6 RV	GATTGGCGATGTAGGACCCAG
SP9 FW	GCCACGTCTATACTCGGG
SP9 RV	GAAGGCGCTCGACTCTG
SNCA FW	AAGAGGGTGTCTCTATGTAGGC
SNCA RV	GCTCCTCCAACATTTGTCACTT
KCNA4 FW	GTACCTCCATGACCCCTCAGA
KCNA4 RV	CTGCCGGTAGTGGGCTTTC
MMP9 FW	TGTACCGCTATGGTTACTACTCG
MMP9 RV	GGCAGGGACAGTTGCTTCT
HAP1 FW	CGGTCTATGCCCGACAATTC
HAP1 RV	GTAGGTTAGGACACAGTGCTTC
BDNF FW	TGGGTGACACTTTCGAACAC
BDNF RV	ATCACCTGGACGTGTACAA
TRKB FW	TTTGTACTGCCTGAATGAAAGC
TRKB RV	TTTGACAGATGGCAAACCAC
AEN FW	CAAGTGTGTGGCTATCGACTG
AEN RV	CACTCCAGCGGGTACGGTA
ITIH5 FW	CCTACTGTAGTACAACAAGCCAG
ITIH5 RV	TCCCAATGCTCTGTTCTCTATT